Use of the Enterprise™ Intracranial Stent for Revascularization of Large Vessel Occlusions in Acute Stroke

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Abstract

Background and Purpose: Major cerebral thromboembolism often resists recanalization with currently available techniques. The authors present their initial experience with a self-expanding stent for use in intracranial vascular reconstruction, permitting immediate recanalization of acute thromboembolic occlusions of the anterior circulation.

Patients and Methods: Patients treated with the Cordis Enterprise™ self-expanding intracranial stent system for acute thromboembolic occlusion of the major anterior cerebral arteries were included. Treatment comprised systemic and intraarterial thrombolysis, mechanical thrombectomy, and stent placement. Stent deployment, recanalization rate by means of Thrombolysis In Cerebral Infarction (TICI) scores and the clinical outcome were all assessed.

Results: Six patients presenting with acute carotid T (n = 2) or proximal middle cerebral artery occlusion (n = 4) were treated. The mean National Institutes of Health Stroke Scale (NIHSS) score at presentation was 14; the mean age was 57 years. Successful stent deployment and immediate recanalization were achieved in all six with a TICI score of ≥ 2. Neither distal emboli nor any procedure-related complications were encountered. One patient developed symptomatic intracerebral hemorrhage and two patients needed decompressive craniectomy after treatment. The mean NIHSS score at 10 days was 10, but only one patient showed a complete recovery at 3 months.

Conclusion: Intracranial placement of the Enterprise™ self-expanding stent has proven to be feasible and efficient in achieving immediate recanalization of occluded main cerebral arteries. The use of antiplatelet therapy after treatment may, however, increase the risk of reperfusion intracerebral hemorrhage.

Key Words: Acute stroke · Intracranial stenting · Revascularization · Thrombolysis · Thrombectomy

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Einsatz des Enterprise-stent-systems zur Rekanalisierung großer intrakranieller Arterien beim akuten Schlaganfall

Zusammenfassung

Hintergrund und Ziel: Die Wiedereröffnung großer thromboembolisch verschlossener Arterien gelingt mit bisherigen endovaskulären Techniken häufig nicht. Die Autoren berichten über ihre Erfahrungen mit einem selbstexpandierenden Stentsystem zur Wiederherstellung des Blutflusses bei Patienten mit akutem thrombembolischem Verschluss in der vorderen Hirnzirkulation.

Patienten und Methodik: Patienten mit Verschluss einer großen Arterie in der vorderen Gerhirnkreislauf, die mit einem Enterprise-Stentsystem (Cordis Enterprise™) behandelt wurden, wurde in diese Studie eingeschlossen. Die Behandlung beinhaltete darüber hinaus eine systemische und intraarterielle Lyse sowie eine mechanische Thrombektomie. Die Stent-

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applikation, die Rekanalisierung unter Verwendung der TICI-Scores (Thrombolysis In Cerebral Infarctions) Scores und der klinische Verlauf wurden analysiert und bewertet.
Ergebnisse: Sechs Patienten wurden eingeschlossen. Zwei Patienten hatten einen Karotis-T-Verschluss und vier Patienten einen Verschluss der A. cerebri media. Der durchschnittliche NIHSS-Score (National Institutes of Health Stroke Scale) Scores betrug bei Aufnahme 14; das mittlere Alter lag bei 57 Jahren. Die Stentapplikation war bei allen Patienten erfolgreich, und eine Rekanalisierung mit einem TICI-Score ≥ 2 konnte in allen Fällen erzielt werden. Distale Emboli und prozedurale Komplikationen traten nicht auf. Im Verlauf erlitt ein Patient eine symptomatische intrazerebrale Blutung, zwei weitere Patienten mussten zur Druckentlastung kraniektomiert werden. Der mittlere NIHSS-Score nach 10 Tagen betrug 10; nur ein Patient zeigte eine komplette Restitution nach 3 Monaten.
Schlussfolgerung: Die intrakranielle Applikation des Enterprise-Stentsystems (Cordis Enterprise™) zur Behandlung großer arterieller Verschlüsse im vorderen Gehirnkreislauf ist möglich und sicher durchführbar. In dieser Serie zeigt sich eine hohe Effizienz mit Reperfusion bei allen Patienten. Die Gabe von Thrombozytenfunktionshemmern erhöht möglicherweise das Risiko einer großen Reperfusionsblutung.

Schlüsselwörter: Akuter Schlaganfall · Intrakranieller Stent · Thrombolyse · Thrombektomie

Introduction

Thromboembolic occlusions of the major cerebral arteries of the anterior circulation, the internal carotid artery (ICA) and the proximal middle cerebral artery (MCA), are conditions that almost always result in severe neurologic compromise. Outcomes are usually poor, with a high mortality rate. Such lesions are often refractory to intravenous and/or intraarterial thrombolysis [1–3]. Furthermore, early reocclusion after intravenous thrombolysis is not infrequent, and is associated with clinical deterioration and poor outcome [4]. The impact of rapid recanalization on improvement of clinical outcome is increasingly recognized [5, 6].

Additional therapeutic options for patients with major vessel occlusion include mechanical thrombectomy. However, for acute stroke patients failing pharmaceutical and mechanical thrombolysis, few alternatives remain. As a complementary treatment, with the advent of self-expanding stents suitable for intracranial delivery, stent application for rapid recanalization of acute intracranial vessel occlusions has resulted in high angiographic success rates [7–12]. We present our initial experience with the off-label use of the Enterprise™ (Codman & Shurtleff, Inc., Raynham, MA, USA) intracranial self-expanding stent for vascular reconstruction in acute stroke.

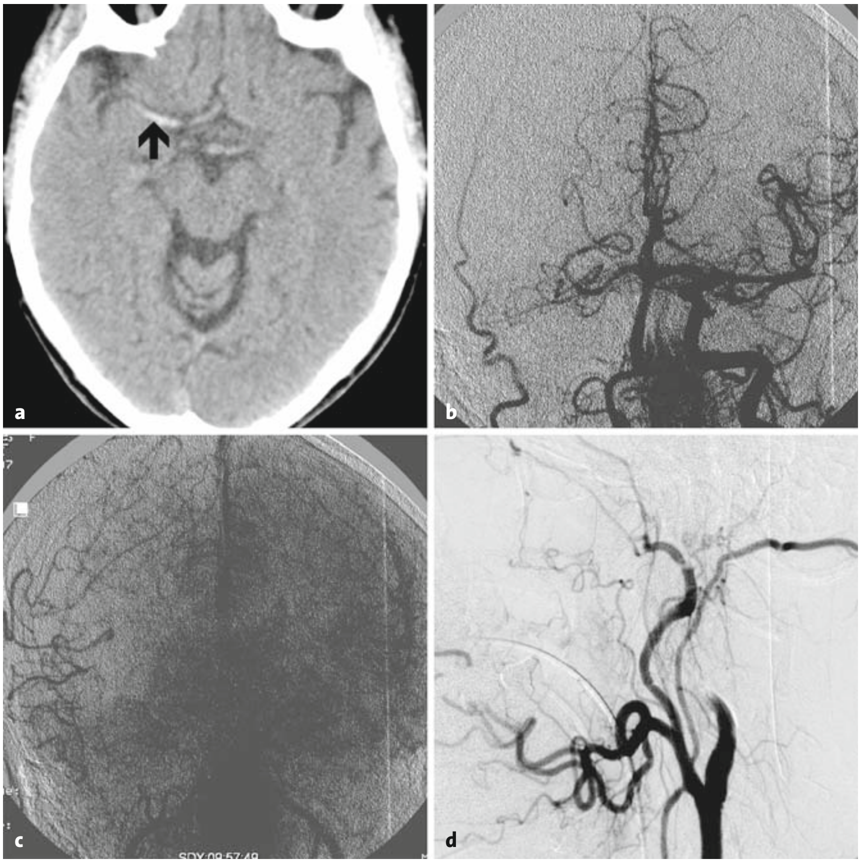
Patients and Methods

From the stroke database of our institution, we retrospectively identified and analyzed those patients, who, by suffering a major anterior circulation acute stroke, were treated with intracranial placement of the Enterprise™ stent, as an off-label use. Between November 2007 and September 2008, altogether six such patients were treated. These patients were diagnosed by computed tomography (CT) and CT angiography to have a major anterior circulation occlusion. Not responding to initial intravenous recombinant tissue plasminogen activator (rtPA) or presenting in a time window excluding access to such treatment by policy of our local stroke center, we requested consent to intraarterial recanalization procedures. After angiographic confirmation of persistent occlusion and failure or impossibility to proceed with mechanical thrombectomy, intracranial vascular reconstruction was performed by stent placement with the Enterprise™ system (Figure 1).

Retrospectively, a database was created with the following characteristics: demographics (age, sex, cardiovascular risk factors), clinical (etiology of stroke, time of symptom onset, baseline and 10-day National Institutes of Health Stroke Scale [NIHSS] scores, symptom onset-to-treatment time, time to revascularization), radiographic and angiographic data (location and extension of clot, pharmacological treatment, and mechanical devices used before and after stenting). The degree of collateral flow was assessed according to the Angiographic Collateral Flow Grading System, where grade 0 means no collateral flow and grade 4 means complete and rapid collateral flow [13]. The degree of recanalization was classified based on the Thrombolysis In Cerebral Infarction (TICI) perfusion categories for reporting purposes [13]. Clinical outcome was assessed by modified Rankin Scale (mRS) at 3 months.

Procedural Technique

Under general anesthesia, a standard 7- or 8-F transfemoral approach was used to access the thrombosed vessel. Initial parenchymography [14] and selective study of the concerned carotid artery allowed for assessment of the occlusion site, as well as of collateral supply.



Figures 1a to 1d. Unenhanced brain CT scan of patient #1 with hyperdense MCA sign (arrow; a). Parenchymography with contrast injection from the aortic arch demonstrating occlusion of the right ICA and MCA with a significant perfusion delay of the right hemisphere (b, c). Lateral view of right common carotid injection showing occlusion of the ICA (d).

Mechanical thrombectomy attempts were made in three cases, having been combined with intraarterial thrombolysis in two patients. In the remaining three cases, due to a combination of anatomic considerations, advanced time and occlusion type, stent positioning was performed alone. The patients received periprocedural heparin for systemic anticoagulation with a bolus dose of 2,000–5,000 IU followed by additional 1,000 IU every 60 min. Immediately before or after stent deployment, intravenous aspirin was administered (250 or 500 mg) and intravenous tirofiban infusion was started adjusted to patients' body weight.

For the performance of intracranial stenting, a 0.014" microwire-guided 0.021" inner diameter-sized Prowler® Select™ Plus microcatheter (Codman & Shurtleff, Inc.) was navigated beyond the site of occlusion, followed by deploying a self-expanding Enterprise™ stent. The length of the stent was chosen to completely cover the occluded vascular segment, and reached from 22 to 37 mm. The decision regarding the duration of treatment with tirofiban and an initiation of clopidogrel was made based on the postprocedural brain CT findings, and by taking the risks of hemorrhagic transformation into consideration.

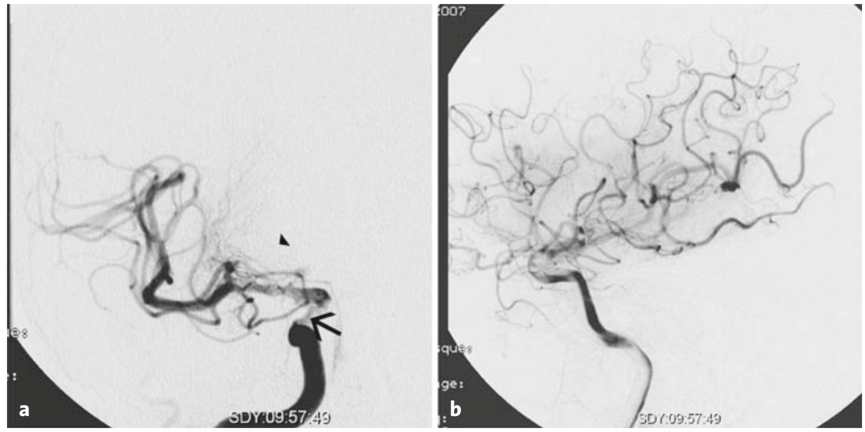
Results

Four female and two male patients with a mean age of 57 ± 13 years presenting with severe acute stroke of the anterior circulation were treated with the Enterprise™ self-expanding stent system between November 2007 and September 2008 at our stroke center. The mean

Table 1. Characteristics of patients undergoing intracranial stenting. F: female; L: left; M: male; NIHSS: National Institutes of Health Stroke Scale; R: right; T: carotid T.

Patient #	Age (years)/ sex	Admission NIHSS score	Stroke etiology	Time elapsed Symptom onset to angiography (h:min)	Angiography to stent deployment (min)	Thrombus location (side)	Grade of collateral circulation
1	61/F	12	Atrial fibrillation	3:29	101	T + M1 (R)	3
2	48/F	16	Carotid dissection	4:48	51	M1 (L)	1
3	43/M	15	Cryptogenic	3:41	42	T + M1 (R)	1
4	49/F	16	Carotid dissection	4:13	35	T + M1 (L)	2
5	66/M	17	Cryptogenic	2:13	103	T + M1 (R)	1
6	76/F	9	Cardioembolic	2:47	120	M1 (L)	2

baseline NIHSS score at presentation was 14 ± 3. After an initial CT, one patient was treated with intravenous rtPA, receiving half of the body-weight-adjusted dose without clinical improvement. The mean time to first angiography was 3 h and 31 min. The baseline demographic data, the clot location, and the grading of collateral circulation are listed in Table 1.



Figures 2a and 2b. Anterior (a) and lateral (b) view of the recanalized right ICA and MCA after stent deployment. Note the residual luminal irregularities still present after stent deployment (arrow) and the opacification of the lenticulostriate arteries (arrowhead).

Unsuccessful mechanical thrombectomy was attempted in one case with the MERCI Retrieval System® (Concentric Medical Inc., Mountain View, CA, USA). The Penumbra System™ (PS; Penumbra Inc., Alameda, CA, USA) was used prior to stenting in two cases. In one of these patients, partial recanalization of the M1 segment was achieved via thromboaspiration; however, the reperfusion catheter could not be introduced in the occluded upper trunk of the MCA bifurcation. The branch was then catheterized with the Prowler® Plus microcatheter, and after unsuccessful local rtPA infusion, it could be recanalized by stent placement. In the second case, no recanalization could be achieved with a combination of PS and intraarterial lysis, so stent placement was used to reopen the occluded carotid bifurcation. In the other four cases, the performing physician decided upon immediate stenting. The occluded segment was recanalized in all cases by a self-expanding Enterprise™ stent of 4.5 mm in diameter and 22, 28 or 37 mm in length chosen depending on the length of the occlusion. In all cases, one stent allowed for covering the concerned vascular segments ranging from the MCA bifurcation to the supraclinoid or cavernous carotid segment, or covering the M2 and M1 segments. The stent placement allowed for immediate revascularization of the occluded segments. The mean time to stent deployment needed from the first angiographic study was 75 ± 34 min, including diagnostic runs and mechanical maneuvers.

After stent deployment, immediate recanalization was observed in all six patients; however, the revascularized vessels exhibited remaining luminal irregularities. This angiographic aspect was further improved upon administration of intravenous aspirin and tirofiban. By the end of the procedure, two patients demonstrated a recanalization grade of 2a, two of 2b, and two of 3 according to the TICI grading system (Figure 2). No procedure-related complications were encountered.

Brain CT scans 24–36 h post treatment demonstrated that three out of six patients developed an infarct affecting more than two thirds of the MCA territory, and one patient developed a capsular, space-occupying intracerebral hematoma. Two patients became candidates for decompressive craniectomy because of a space-occupying edema developed a few days after stroke onset, and one of them required repeated decompression because of a postoperative intracerebral hematoma that occurred 1.5 h after craniectomy. The mean NIHSS score at 10 days was 10 (range 0–17). Two patients exhibited an improvement of > 2 points on the NIHSS. One patient showed a complete recovery with an mRS of 0, and two patients were dead at the 3-month follow-up. One of them, although improved from an initial NIHSS score of 9 to 3 after thromboaspiration, died of a malignancy before the 3-month follow-up (Table 2). The stroke-related mortality was 16%.

Discussion

Current reported clinical experience reveals that occlusions of the intracranial ICA and the M1 segment of the MCA are highly resistant not just to intravenous thrombolysis [15], but also to intraarterial pharmacological and mechanical recanalization efforts [16, 17]. It is well known, that carotid T and complete M1 segment occlusions have the highest morbidity and mortality rates with less favorable clinical outcome [3, 18–20]. It has also been demonstrated that early recanalization is strongly related with better clinical outcome [5, 6, 16].

Table 2. Procedure and postprocedure data. mRS: modified Ranking Scale; NIHSS: National Institutes of Health Stroke Scale; PS: Penumbra™ System; rtPA: recombinant tissue plasminogen activator; TICI: Thrombolysis In Cerebral Infarction.

Patient #	Treatment received	TICI post procedure	Craniectomy	Clinical outcome 10-day NIHSS score	3-month mRS score
1	MERCI	3	No	0	0
2	Intravenous rtPA	2a	Yes	14	4
3	No	2b	No	13	3
4	No	2a	Yes	13	4
5	PS	2b	No	17	6
6	PS	3	No	3	6

The pooled analysis of the two MERCI trials has shown that best results were achieved with combined thrombectomy and thrombolytic maneuvers in patients with ICA occlusions, however, with recanalization rates limited to less than two thirds of patients [21]. Another mechanical thrombectomy device, the PS, has also shown promising results in terms of revascularization and clinical outcome, with recanalization results ranging between 82% and 100% [22–24]. Despite the improving revascularization results, obviously not many options remain for the relatively high percentage of patients where the currently accepted mechanical and chemical thrombolytic attempts fail.

One solution for this group is recanalization using intracranial stents. After the advent of the intracranially trackable balloon-mounted stents and, later, the self-expanding intracranial stents, attempts were made to use these devices in recanalization procedures of intracranial arterial occlusions. There are few case reports and series demonstrating that these devices are effective in the recanalization of vascular occlusion with a relatively high angiographic success rate [7–12, 25–27]. In the multicenter cases series of Levy et al., who treated 18 such patients, the authors reported a 79% recanalization rate of TICI 2/3 [25]. In this case series, only three out of seven patients presenting with involvement of the ICA could be recanalized with stent placement, but vessel reconstruction to a TICI 2/3 degree could be achieved in all patients showing solitary M1 occlusions. Significant clinical improvement of > 4 points on the NIHSS was observed only in seven out of 14 patients, where a TICI 2/3 grade recanalization could be achieved [25]. In a recently published series comprising twelve acute stroke patients, the authors reported on the use of the Wingspan™ stent for revascularization. In this series, five patients had an occlusion of the M1 or M2 segment of the MCA. Four of them had a partial recanalization of TIMI 2 or 3 degree, but only one patient showed a favorable outcome at 3 months [12]. These results demonstrate that revascularization efforts with available intracranial stents are not always successful. In a very recent multicenter study, the authors evaluated the use of the Enterprise™ stent as a salvage revascularization tool, after routine interventions aiming at recanalization had been unsuccessful. In this series, a TIMI 2/3 recanalization rate of 100% was achieved with 75% of patients showing at least 4-point improvement on the NIHSS [28].

The Enterprise™ self-expanding vascular reconstruction system was designed specifically for brain aneurysm repair. The stent has a closed-cell design with flared ends, which are both aspects we consider of advantage when it comes to trapping a clot toward the vessel wall. Given its maximum available length of 37 mm, this device is long enough to cover extensive lesions without the need for multiple stent deployment. The stent was deployed in all of our cases starting from the MCA bifurcation to the supraclinoid or cavernous portion of the ICA covering the whole occluded segment. The stent delivery Prowler® Select™ Plus microcatheter was easy and atraumatic to navigate in the cerebral vasculature and the stent was easy to deliver even in patients with tortuous precerebral and intracranial vessel anatomy. By its radial force, the stent was able to partially reconstruct the occluded vessels immediately after deployment, and the residual luminal irregularities further improved with the administration of aspirin and tirofiban. The mean time to stent deployment and thus to recanalization was relatively short. The stent delivery and deployment did not produce any visible clot fragmentation, and there were no signs of late embolization in patients not suffering a major infarct. This was impossible to exclude in patients developing an infarct of more than two thirds of the MCA territory. In two cases, the stent caged the origin of an M2 branch, which remained occluded by clot at the immediate follow-up angiograms (patients with a TICI 2a recanalization). We suggest the immediate recanalization of the carotid artery and MCA in all of our patients to be attributable to the fact, that the stent was long enough to cover extended occlusions, and by its closed-cell design and radial force was able to compress and trap the thrombus.

There are, however, two major concerns using intracranial stents for acute recanalization in ischemic stroke. One of them is the fear of side branch and perforator occlusion; opening the stent inside the thrombus might cause "snow-plowing" of the clot into side branches or perforating arteries. In complete carotid and/or M1 segment occlusions, the arising branches covered by thrombus are already occluded, so if it were a case of pushing the thrombus further along these vessels, the situation would not get any worse. On the contrary, we believe that the anatomic vascular configuration forces the intracranial microdevices to track in close proximity to the vessel wall, i.e., along the outer curve (in the case of the carotid artery and the M1 segment, where the posterior communicating, the anterior choroidal and the lenticulostriate arteries arise). Based on this concept, the microcatheter with the stent will be navigated between the vessel wall and the thrombus and not inside the clot itself. With deployment, the stent will push away the clot from the origin of the perforators and trap it against the opposite wall at the inner curve. We could indeed demonstrate the reappearance of the lenticulostriate arteries in all of our cases (see Figure 2a). The reperfusion of perforators was also demonstrated in a similar patient series [12].

The other concern is related to the need for antiplatelet therapy after stent deployment, in view of the risk of intracerebral hemorrhage (ICH). On the one hand, the risk of combined antiplatelet therapy in acute stroke is not extensively studied and thus not recommended by the current guidelines [29]. The risk of ICH may be further increased if tPAs were concomitantly used [29, 30]. However, stent deployment with antiaggregant therapy was occasionally used in combination with plasminogen activators in the above-mentioned case series [8–10]. On the other hand, the use of antiplatelet therapy might constitute a problem in cases when patients require neurosurgical intervention such as decompressive craniectomy or hematoma evacuation. In our case series, there was a relatively high incidence of ICH after revascularization. One patient developed a space-occupying hematoma 15 h after stent implantation, which did not cause a worsening in his NIHSS score of 17. Another patient suffered a symptomatic ICH 5 days after recanalization, soon after a decompressive craniectomy. Both patients were receiving oral aspirin and clopidogrel treatment.

Despite successful recanalization, there were only two patients showing an improvement of > 4 points on the NIHSS. The explanation for the relatively poor outcome of our patient series may rely on the quality of collateral supply of the suffering brain. Although recanalized within a 6-h time window, all four patients with poor clinical outcomes had insufficient collateral circulation of grade 1 or 2, according to the angiographic assessment (Table 1).

A low patient number limits this study, as does its retrospective nature. It is hoped that a prospective study with a larger sample size might result in more clarity in order to determine the efficacy of self-expanding stents for acute intracranial vascular thrombosis.

Conclusion

In the setting of acute ischemic stroke caused by thromboembolic occlusion of the intracranial ICA or complete M1 segment of the MCA, where chances of recanalization by the currently accepted methods are limited, intracranial vessel reconstruction by self-expanding stents seems to be feasible and angiographically efficient. Our initial experience with the Enterprise™ self-expanding stent used for intracranial vascular reconstruction showed a high potential to reach immediate recanalization of acute major thromboembolic occlusions. These results indicate that primary stenting might have a role in the treatment of acute strokes, where currently accepted modalities fail. The criteria for this kind of treatment should, however, be well delineated to overcome the difficulties and possible complications arising with the use of antiplatelet therapies in cases where huge infarction develops despite successful recanalization. The collateral circulation through corticocortical anastomoses seems to have a crucial importance in achieving better clinical outcomes after revascularization.

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Conflict of Interest Statement

The authors declare that there is no actual or potential conflict of interest in relation to this article.

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